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RESEARCH ARTICLE

SinoSCORE: a logistically derived additive prediction model for post-coronary artery bypass grafting in-hospital mortality in a Chinese population

Zhe Zheng (✉)*[,a], Lu Zhang*, Xi Li, Shengshou Hu (✉)[b]; on behalf of the Chinese CABG Registry Study

Department of Cardiovascular Surgery and State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100037, China

Abstract **This study aims to construct a logistically derived additive score for predicting in-hospital mortality risk in Chinese patients undergoing coronary artery bypass surgery (CABG). Data from 9839 consecutive CABG patients in 43 Chinese centers were collected between 2007 and 2008 from the Chinese Coronary Artery Bypass Grafting Registry. This database was randomly divided into developmental and validation subsets (9:1). The data in the developmental dataset were used to develop the model using logistic regression. Calibration and discrimination characteristics were assessed using the validation dataset. Thresholds were defined for each model to distinguish different risk groups. After excluding 275 patients with incomplete information, the overall mortality rate of the remaining 9564 patients was 2.5%. The SinoSCORE model was constructed based on 11 variables: age, preoperative NYHA stage III or IV, chronic renal failure, extracardiac arteriopathy, chronic obstructive pulmonary disease, preoperative atrial fibrillation or flutter (within 2 weeks), left ventricular ejection fraction, other elective surgery, combined valve procedures, preoperative critical state, and BMI. In the developmental dataset, calibration using a Hosmer-Lemeshow (HL) test was at $P = 0.44$ and discrimination based on the area under the receiver operating characteristic curve (ROC) was 0.80. In the validation dataset, the HL test was at $P = 0.34$ and the area under the ROC (AUC) was 0.78. A logistically derived additive model for predicting in-hospital mortality among Chinese patients undergoing CABG was developed based on the most up-to-date multi-center data from China.**

Keywords coronary artery bypass grafting; risk stratification; in-hospital mortality

Introduction

Risk stratification is of great importance for cardiac surgery [1]. Since the 1980s, several risk models have been established worldwide. Most of these models are logistic or Bayesian, which require complex calculations, and some are proprietary [2–4]. Among these models, EuroSCORE [5,6] was proven successful because of its simplicity and openness. However, several recent studies have found that this widely adopted model overestimates mortality [7–9]. This result may be attributed to differences between Chinese and Western populations and the improved operative outcomes over the decade years. In recent years, the developed off-pump technique, myocardial protection technology, and the improved off-pump technique significantly reduce in-hospital mortality.

The incidence of coronary artery disease (CAD), known as the “epidemiological transition,” is greatly increasing in China [10]. Accordingly, the number of patients who need revascularization via coronary artery bypass surgery (CABG) dramatically increased [11]. This increase is due to the unavailability of a published operative risk model specifically developed for the increasing number of patients in China undergoing CABG. Creating a model is especially important because recent literature reported that EuroSCORE overestimates in-hospital mortality for this cohort of patients [12]. Consequently, we were unable to determine the actual risk of the patients using the EuroSCORE model, which will waste medical resources. This study aims to develop a logistically

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Correspondence: [a]zhengzhe@fuwai.com; [b]shengshouhu@yahoo.com

*Both authors contributed equally to this manuscript as first co-authors.

derived additive model for estimating post-CABG in-hospital mortality based on a large, multi-center Chinese database that accurately assesses the risk among Chinese bypass patients and guides clinical work.

Methods

The Chinese CABG Registry [13] is a national multi-center study that primarily aims to construct a new risk stratification system for Chinese patients undergoing CABG. Its steering group includes a number of Chinese cardiac surgeons and epidemiologists with interest in predicting surgical outcomes in the Fuwai Hospital. All patients (n = 9839) who underwent CABG at 43 participating institutions all over China between January 2007 and December 2008 were enrolled. Detailed information on patient demographics, preoperative risk factors, operative risk factors, and in-hospital mortality was collected. The data collected from the registry included 67 preoperative factors and 30 operative parameters (Table 1) that were selected based on our clinical experience and on prior published CABG risk-prediction models.

The Chinese CABG Registry database was carefully examined and patients < 18 years old and patients with incomplete data records were excluded. Among the patients, 1 was excluded for being < 18 years old and 274 were excluded because of incomplete data. Of the patients with incomplete data, 5 had no age, 70 had no body weight, 52 had no height, 205 had no ejection fractions, 1 did not have information on unstable angina, 2 had no information on cardiogenic shock, and 80 had no NYHA staging. Some overlaps in the data were also observed. A total of 275 patients (6 patients died) were excluded from the study, and 9564 patients were analyzed. The 9564 patients were randomly divided into two subsets with a 9:1 ratio according to method used to develop the EuroSCORE model [6]. These subsets were the developmental dataset (n = 8602), which was used to construct the risk model, and the validation subset (n = 962), which was used to test and validate the model. SPSS 13.0 (SPSS Inc., Chicago, Illinois) was used to perform the statistical analysis. This study was approved by the local IRB/EC (IRB/EC of Fuwai Hospital; approval number: 219).

In the developmental dataset, all the possible risk factors associated with early mortality were screened using chi-square tests for categorical covariates and t-tests or Wilcoxon rank sum tests for continuous covariates. Variables with P values > 0.2 were excluded. A stepwise multivariate logistic regression was performed using the backward method (criteria for entry and removal of variables were 0.05 and 0.10) with one variable eliminated at a time. The stability of the model was checked every time a variable was eliminated. When all statistically non-significant variables were eliminated, a Hosmer-Lemeshow (HL) chi-square test was used to evaluate the calibration. The area under the ROC curve (AUC) was utilized to assess the discriminatory power. In the final score (that is, the SinoSCORE), the weights attributed to each variable were obtained from the logistic regression b coefficients. The multicollinearity of the models was checked using tolerance and inflation statistics. The calibration and discriminatory power were then tested in the validation dataset. This logistically derived additive model was then applied to the entire population (developmental and validation cohorts) divided into three risk levels.

Table 1 Sixty-seven preoperative risk factors for univariate analysis (Part 1/2)

Variable	Definition
Gender	
Age	In years at most recent birthday
Height	
Weight	
BMI	Body mass index
BSA	Body surface area
History of smoking	Prior history of smoking, regardless of whether the patients quit smoking
Family history of coronary artery diseases	Immediate family members diagnosed with coronary artery diseases or had sudden cardiac death with unknown etiology before the age of 55 years old
Diabetes mellitus	Documented past history or fulfilled the criteria of WHO 1999
Hyperlipidemia	Documented past history or TC>5.18 mmol/L, and/or LDL⩾3.37 mmol/L, and/or HDL<0.78 mmol/L, and/or triglyceride>1.69 mmol/L
Hypertension	Documented past history or SBP>140 mmHg and/or DBP>90 mmHg
Chronic renal failure	Documented past history or any previous serum creatinine>176 μmol/L
Cerebrovascular accident	Documented past history of coma⩾24 h or central nervous system dysfunction⩾72 h
Endocarditis	Documented history or diagnosed with blood culture and UCG
COPD	Long-term use of bronchodilators or steroids for lung disease
Immunosuppressive therapy	Any immunosuppressive therapy within 30 days before surgery
Extracardiac arteriopathy	Any one or more of the following: claudication, carotid occlusion or>50% stenosis, previous or planned intervention on the abdominal aorta, limb arteries, and carotid arteries

(*Continued*)

Variable	Definition
Previous cardiac surgery	Requiring opening of the pericardium
Previous CABG	Requiring opening of the pericardium
Previous valve surgery	Surgical procedures with either valve
Previous percutaneous balloon valvuloplasty	Documented history
Previous PCI	Documented history
Previous permanent pacemaker implantation	Documented history
Previous history of non-cardiac surgery	Documented history
History of myocardial infarction	Documented history or ECG evidence
Recent myocardial infarction	$<$21 days
Heart failure	Within 2 weeks
Unstable angina	Resting angina requiring i.v. nitrates until arrival in the anesthetic room
Cardiogenic shock	Lasting until arrival in the anesthetic room
Cardiopulmonary resuscitation	Within 2 h
Preoperative persistent ventricular tachycardia or fibrillation	Within 2 weeks
Preoperative III auriculo-ventricular block (AVB)	Within 2 weeks
Preoperative atrial fibrillation or flutter	Within 2 weeks
Preoperative critical stage	Any one or more of the following: preoperative cardiogenic shock, ventricular fibrillation or flutter, and preoperative IABP implantation
NYHA staging	NYHA definition
Killip staging	For patients with acute MI
CCS staging	For patients with angina
Serum creatinine	Measured before surgery
Total cholesterol	Measured before surgery
Triglyceride	Measured before surgery
LDL	Measured before surgery
HDL	Measured before surgery
Hemoglobin	Measured before surgery
High-sensitivity C-reactive protein (hsCRP)	Measured before surgery
Erythrocyte sedimentation rate (ESR)	Measured before surgery
Left carotid artery lesion	Diagnosed using US or arteriography
Right carotid artery lesion	Diagnosed using US or arteriography
Left renal artery stenosis	Diagnosed using US or arteriography
Right renal artery stenosis	Diagnosed using US or arteriography
Number of involved coronary arteries	Diagnosed using arteriography
Left main stenosis	$\geqslant$50%
Left descending stenosis	$\geqslant$50%
Circumflex stenosis	$\geqslant$50%
Right coronary stenosis	$\geqslant$50%
Graft stenosis	For patients with previous CABG
Ejection fraction	Assessed by echocardiography (measured before surgery)
Ventricular aneurysm	Diagnosed using by UCG
Pulmonary hypertension	Systolic PA pressure$>$ 60 mmHg
Valve stenosis or insufficiency	Either valve
Aortic stenosis	Diagnosed using UCG
Mitral stenosis	Diagnosed using by UCG
Tricuspid stenosis	Diagnosed using UCG
Pulmonary stenosis	Diagnosed using UCG
Aortic insufficiency	Diagnosed using UCG
Mitral insufficiency	Diagnosed using UCG
Tricuspid insufficiency	Diagnosed using UCG
Pulmonary insufficiency	Diagnosed using UCG

Table 1 Thirty operative risk factors for univariate analysis (Part 2/2)

Variable	Definition
Non-elective surgery	Excludes emergency or salvage surgery. Emergency is defined as unscheduled surgery required on the same day because of refractory angina despite maximal medical therapy, acute evolving myocardial infarction within 24 h before surgery, aortic dissection, PCI failure, or other reasons. Salvage surgery is for patients who had cardiopulmonary resuscitation before arrival in the anesthetic room.
On-pump surgery	With extracorporeal circulation
Time of extracorporeal circulation	In minutes
Time of aortic clamp	In minutes
Beating heart surgery	Considered as “beating” for on-pump surgery with ventricular fibrillation
Site of cannula	For on-pump patients
Aortic clamp	Including no clamp, partial clamp, and complete clamp
Intra-aortic balloon pump (IABP) support during or after CABG	Not including preoperative IABP
Ventricular assist device (VAD)	With the aid of ventricular assistance device
Heart transplantation	Heart transplant
Extracorporeal membrane oxygenation (ECMO)	With the aid of ECMO
Number of grafts	Including arterial and venous grafts
Combined valve surgery	Surgical procedures with either valve
Procedure on aortic valve	Including repair, replacement, and any other procedures
Procedure on mitral valve	Including repair, replacement, and any other procedures
Procedure on tricuspid valve	Including repair, replacement, and any other procedures
Procedure on pulmonary valve	Including repair, replacement, and any other procedures
Repair for ventricular aneurysm	Including any kind of repair
Repair of septal rupture	Repair of septal rupture
Excision of heart tumor	Excision of heart tumor
Repair of congenital heart defects	Including VSD/ASD repair and others
Laser drilling	Laser drilling
Repair of injured cardiac muscle	Procedure for the repair of injured heart muscle
Implantation of permanent pacemaker	Implantation of permanent pacemaker
Surgery for atrial fibrillation	Including Maze procedure or other radio frequency ablation
Thoracic aorta procedure	For disorders of the ascending, arch, or descending aorta
Cell transplantation	Via coronary injection or direct injection
Hybrid procedure	Planned hybrid procedure with PCI and CABG
Carotid procedure	Including stent implantation and CEA
Post-infarct septal rupture	

Results

A total of 9839 patients from 43 surgical centers in 16 provinces in China participated in the project. After error checking and quality control procedures, 9564 patients were analyzed. Elective procedures were 97.1%, and isolated CABG accounted for 87.7%. Overall in-hospital mortality was 2.5%.

Patient characteristics

The mean age was 62.1 years old, with a standard deviation of 9.2 and 77.3% were male. The mean BMI was 25.1 $\pm$ 3.3 with 62.6% $>$ 24 and 1.1% $<$ 18. A history of hypertension occurred in 37.0% of patients. Diabetes was present in 29.8% of patients, with 5.7% on diet control, 17.5% on oral therapy, and 6.6% on insulin.

Construction of the SinoSCORE

Risk factor identification

Multivariate analysis identified 11 risk factors that are related to in-hospital mortality. These factors were classified into three groups, namely, patient related, cardiac, and operation related (Table 2). Multicollinearity diagnostics with tolerance statistics ruled out the multicollinearity of the 11 factors.

Table 2 Risk factors and weights

Risk factor	Definition	*P* value	Score
Patient-related factors			
Age 65–69	In years	<0.001	3
70–74		<0.001	5
⩾75		<0.001	6
BMI⩾24	BMI	0.019	−2
BMI<18		0.002	5
Chronic renal failure	Documented past history or any previous serum creatinine>176 μmol/L	<0.001	6
Extracardiac arteriopathy	Any one or more of the following: claudication, carotid occlusion or>50% stenosis, previous or planned intervention on the abdominal aorta, and limb arteries or carotids	0.011	5
Chronic obstructive pulmonary disease	Long-term use of bronchodilators or steroids for lung disease	0.024	4
NHYA stage III	NHYA definition	<0.001	3
NHYA stage IV		<0.001	7
Cardiac factors			
Preoperative atrial fibrillation or flutter	Within 2 weeks	0.035	2
Ejection fraction<50%	Assessed by echocardiography (measured before surgery)	<0.001	4
Preoperative critical stage	Any one or more of the following: preoperative cardiogenic shock, ventricular fibrillation or flutter, and preoperative IABP implantation	<0.001	4
Operation-related factors			
Non-elective surgery	Non-elective procedure	<0.001	5
Combined valve surgery	Surgical procedures with either valve	<0.001	4

Risk model construction

Table 3 and Fig. 1 list the statistical features of the developmental and validation datasets. The validation analysis proved that the calibration of the model was satisfactory and the discrimination power was characterized by an AUC of 0.80. This system, which is similar to the EuroSCORE, is additive.

Risk model application

The SinoSCORE was applied to the whole database. The patients were divided into three risk groups according to the risk scores (Table 4). The observed and predicted mortalities overlapped in all risk groups.

Discussion

Necessity of developing a Chinese model

The incidence of CAD in China is increasing dramatically, with an estimated CAD incidence rate as high as 98 per 100 000 [10]. This rate might increase by > 50% from 2010 to 2030 [14]. Although this incidence rate is lower compared with that in the US, considering the large population of China (more than 1300 million), the number of new CAD patients and patients who need revascularization via CABG in China is considerably high and rapidly increasing. The last decade has witnessed immense advances in surgical, anesthetic,

Table 3 Statistical features of datasets in SinoSCORE

Dataset	Patients	Calibration chi-square (Hosmer-Lemeshow)	Discrimination area under the ROC curve
Developmental	8602	0.44	0.80
Validation	962	0.34	0.78

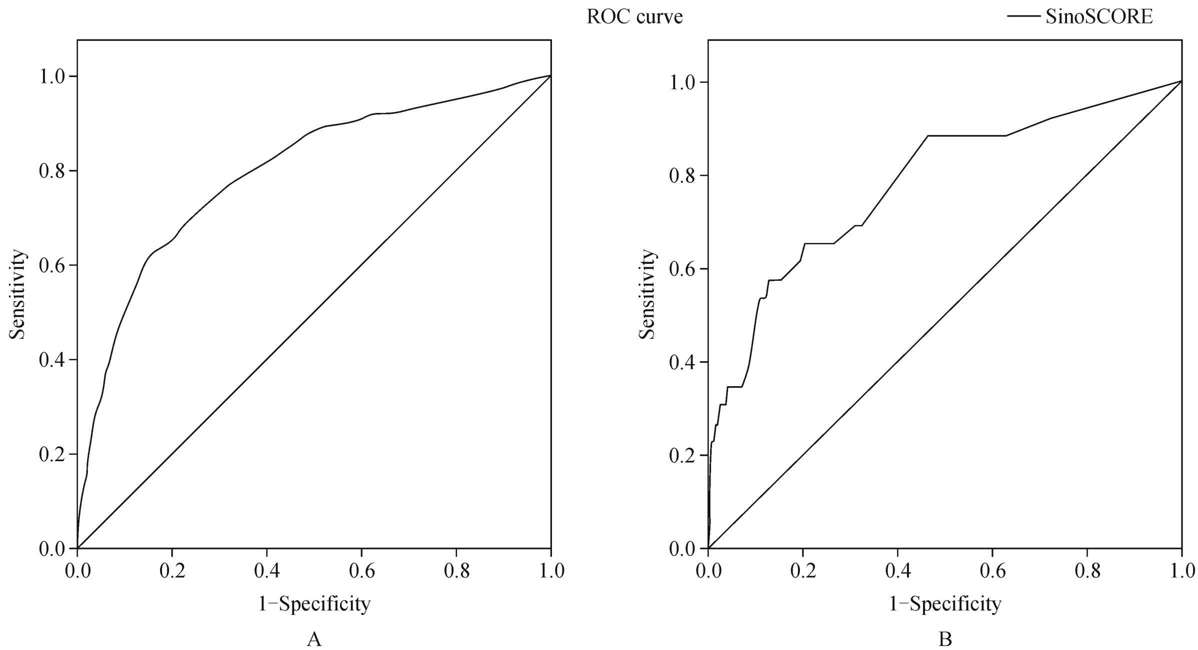

Fig. 1 (A) ROC curve for SinoSCORE in the developmental dataset; (B) ROC curve for SinoSCORE in the validation dataset.

Table 4 Application of SinoSCORE

SinoSCORE	Patients	Died	95% CI	
			Observed**	Expected***
⩽1* (Low risk)	4082	23	0.37–0.81	0.52–0.89
2–5* (Medium risk)	2920	44	1.13–1.98	1.29–1.94
⩾6* (High risk)	2562	176	5.00–7.89	6.36–6.63
Total	9564	243	2.25–2.86	2.48–2.60

Note: *The numbers indicated SinoSCORE values.
**The 95% CIs are based on the mean risk observed for patient groups with different surgical risks.
***The 95% CIs are based on the mean risk predicted for the risk class group using SinoSCORE.

perfusion procedures, and postoperative intensive care worldwide [11]. Considering most of the existing risk prediction models were developed more than a decade ago and are based on large populations in Europe and the US, developing a risk stratification system applicable for contemporary Chinese patients is highly appropriate. This necessity is further supported by three reasons. First, some of the existing risk models, such as the proprietary model of the Society of Thoracic Surgeons (STS) from the USA, are proprietary and unavailable to Chinese clinicians [15]. Second, open models such as EuroSCORE, which is based on European populations, has been proven unsuitable for Chinese CABG patients [12]. Third, most of the previous models are based on Western populations and the difference between Chinese and Western populations highlights the need to construct a model for Chinese patients. Comparison of the demographic characteristics of the study population based on the EuroSCORE multinational database revealed that 43.6% had hypertension and 16.7% had diabetes [16], whereas the SinoSCORE database indicated 37.0% had hypertension and 29.8% had diabetes.

This study, based on the largest most up-to-date multicenter database in China, is the first attempt to develop a risk stratification system for Chinese CABG patients. To our knowledge, this is the first risk stratification model for CABG patients in Asia, the largest continent and home to more than two-thirds of the world's population. This model is worth validating in other Asian countries or among migrants of Asian origin in Western countries.

Logistically derived model

The SinoSCORE model incorporates 11 variables, which were mostly included in previous models [3,4,6]. However, our model differs with other existing models in at least two aspects. First, re-operation ("previous cardiac surgery" or “previous CABG”) was included for analysis (Table 1), but was not as a major risk factor, in the Chinese model. However, this factor was given a heavy weight in non-Chinese models. This result might be due to population differences and the fact that patients with previous cardiac surgery accounted for a very small proportion in our cohort. Previous cardiac surgery accounted for 1.1%, whereas previous CABG accounted for 0.3%. These low re-operation rates reflect the current situation in China (perhaps as well as in other developing countries where CAD is becoming increasingly prominent). The second difference is the high percentage of off-pump procedures (52.4%) in our cohort. Many of the existing models were constructed based on data more than a decade ago [3,6] during which the off-pump technique was uncommon. These models do not reflect the advances in surgical techniques during the past 10 years, especially the introduction of off-pump surgery. Moreover, the percentage of off-pump CABG was much lower in Western populations. The 1998–2009 Nationwide Inpatient Sample databases from the USA identified 3 046 709 patients who underwent CABG procedures, 744 636 (24.4%) of whom were off-pump CABG [16]. Thus, our study constructed a model from a population with a majority of patients undergoing off-pump CABG, which contributes to existing literature.

The effects of off-pump procedures on operative mortality have been debated. One prospective randomized trial [17] demonstrated that off-pump CABG does not differ significantly from on-pump CABG in terms of 30-day composite outcome (death and major complications). The latest study “CORONARY,” the largest trial yet conducted, compared the performance of off-pump CABG with on-pump CABG. The study reported that off-pump CABG has a better safety and efficacy [18]. Our study indicated that off-pump CABG was not a risk factor for post-CABG in-hospital mortality.

Limitations

This study utilized in-hospital mortality as the major endpoint, whereas the EuroSCORE model used 30-day mortality as the endpoint [6]. The difference between the different models determined using this study might be due to differences in the endpoints. However, the use of in-hospital death as the endpoint is justified by the following reasons. First, other studies also used in-hospital mortality [19,20]. Second, the length of postoperative hospital stay is much longer in China than the US and Europe: the mean postoperative length of stay (PLOS) in our study population was 13.5 days, whereas a study that utilized data (496 797 procedures from 1997 to 2001) from the STS database had a mean PLOS of 6.9 days [21]. Third, out of hospital postoperative death in China within 30 days is very unusual because of the lack of extended care and ventilator facilities compared with the US and Europe.

The results of this study were not validated using external data; thus, the SinoSCORE model should be applied to non-Chinese populations with great caution. Similarly, using models developed in the US and European populations may not be as accurate when applied to a contemporary Chinese population. Thus, our model may not be applicable to other populations and requires further validation.

This model is a logistically derived additive model. Given that categorization of continuous data might cause information loss, a logistic model that incorporates continuous variables without dichotomization would be more accurate. However, a considerable number of hospitals in China do not have access to the sophisticated information technology and need to utilize a logistic model. Thus, a logistically derived additive model that is easy to use for most Chinese doctors is preferred. This approach exhibits good discrimination and calibration of the current additive model. Considering the rapid development of the Chinese economy and the exponential growth of IT technology, we anticipated that a logistic model with better accuracy would be available in most Chinese centers in the future.

Conclusions

SinoSCORE, an 11-variable logistically derived additive model, was developed to predict in-hospital mortality among Chinese patients undergoing CABG. This model was based on the most recent multi-center data in China.

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The 43 centers (alphabetical order) that participated in the Chinese CABG registry study (2007–2008) were as follows:
Beijing University First Hospital, Beijing University People’s

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Compliance with ethics guidelines

Zhe Zheng, Lu Zhang, Xi Li, and Shengshou Hu declare no conflicts of interest. This study was approved by the ethics committee of Fuwai Cardiovascular Hospital.

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